Media Release

Furnished under Rule 12g3-2(b) ROCHE HOLDING 82-3315

Roche



DEC 2 1 2006

Basel, 11 December 2006

Xeloda meets primary endpoint in multinational Phase III advanced colorectal cancer study

Roche to approach world-wide regulatory authorities for a new file submission

Roche announced today that a large, international Phase III study (NO16967) of 627 previously treated patients with advanced colorectal cancer met its primary endpoint of progression-free survival. Study results showed that the chemotherapy combination XELOX (oral Xeloda plus oxaliplatin) is as effective in delaying disease progression as the chemotherapy combination FOLFOX-4 (infused 5-FU/leucovorin plus oxaliplatin).

"This data endorses previous findings that oral Xeloda in combination with exaliplatin may provide a new treatment choice for colorectal cancer patients" said Eduard Holdener, Head of Global Development at Roche. "These data will be used in the submission to worldwide regulatory authorities to allow patients with colorectal cancer the opportunity to have an effective at PROCESSED convenient therapy."

JAN 0 4 2007

Xeloda is an oral chemotherapy that can be taken at home and as such it has an important convenience benefit for both patients and doctors compared to intravenous infusions which requirement multiple hospital visits. This targeted cancer medicine is already used in previously untreated colorectal cancer patients and last year Xeloda received the additional approval for the treatment of early (adjuvant) colon cancer.

Results from the NO16967 study will be submitted for presentation at future major medical meetings.

"Our data complement the findings of the NOI6966 study, suggesting that XELOX is a very reasonable treatment option for patients with recurrent colorectal cancer," said Mace Rothenberg, MD, lead investigator and Professor of Medicine at Vanderbilt University Medical Center and

F. Hoffmann-La Rocho Ltd

4070 Basel, Switzerland

Corporate Communications

Tel. ++41-61-686 68 88 Fax ++41-61-686 27 75 http://www.rocho.com Ingram Professor of Cancer Research at Vanderbilt-Ingram Cancer Center. "By demonstrating that Xeloda in combination with oxaliplatin was as effective as FOLFOX-4, these two studies provide the strongest evidence yet that Xeloda may be used in place of IV 5-FU in the treatment of patients with advanced colorectal cancer."

In 2004, colorectal cancer was one of the leading cancers and accounted for 13 percent of all cancers. It is estimated that more than 394,000 people die worldwide from colorectal cancer each year.<sup>2</sup>

# About the Study

The NO16967 trial is a large, international phase III trial which randomized 627 patients from 15 countries world-wide who had previously received chemotherapy and whose disease had returned or continued to progress.

The primary objective was to answer whether the XELOX regimen (Xeloda plus oxaliplatin) is as effective as FOLFOX 4 (intravenous bolus and infusional 5-fluorourseil/leucovorin plus oxaliplatin) in delaying disease progression or death. The secondary outcomes, to be reviewed included overall survival, overall response rates, and safety profile.

#### About XELOX

An abbreviation for a type of combination chemotherapy used to treat colorectal cancer; it contains Xeloda (capecitabine) plus oxaliplatin.

# About Xeloda (capecitabine)

Xeloda is licensed in more than 90 countries worldwide including the EU, USA, Japan, Australia and Canada and has been shown to be an effective, safe, simple and convenient oral chemotherapy in treating over 1 million patients to date.

Roche received marketing authorisation for Xeloda as a first-line monotherapy (by itself) in the treatment of metastatic colorectal cancer (colorectal cancer that has spread to other parts of the body) in most countries (including the EU and USA) in 2001. Xeloda has also been approved by the European Medicines Agency (EMBA) and U.S. Food and Drug Administration (FDA) for adjuvant (post-surgery) treatment of colon cancer in March and June 2005, respectively.

Xeloda is licensed in combination with Taxotere (docetaxel) in women with metastatic breast cancer (breast cancer that has spread to other parts of the body) and whose disease has progressed following intravenous (i.v.) chemotherapy with anthracyclines. Xeloda monotherapy is also

indicated for treatment of patients with metastatic breast cancer that is resistant to other chemotherapy drugs such as paclitaxel and anthracyclines. Xeloda is licensed for the first-line treatment of stomach cancer that has spread, in South Korea.

The most commonly reported adverse events with Xeloda include diarrhoea, abdominal pain, nausea, stomatitis and hand-foot syndrome (palmar-plantar erythrodysesthaesia).

#### About Roche

Headquartered in Basel, Switzerland, Roche is one of the world's leading research-focused healthcare groups in the fields of pharmaceuticals and diagnostics. As a supplier of innovative products and services for the early detection, prevention, diagnosis and treatment of disease, the Group contributes on a broad range of fronts to improving people's health and quality of life. Roche is a world leader in diagnostics, the leading supplier of medicines for cancer and transplantation and a market leader in virology. In 2005 sales by the Pharmaceuticals Division totalled 27.3 billion Swiss francs, and the Diagnostics Division posted sales of 8.2 billion Swiss francs. Roche employs roughly 70,000 people in 150 countries and has R&D agreements and strategic alliances with numerous partners, including majority ownership interests in Genentech and Chugai. Additional information about the Roche Group is available on the Internet (www.roche.com).

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#### Additional information

- Roche in Oncology: www.roche.com/mboncology-e.pdf
- Roche Health Kiosk, Cancer: www.health-kiosk.ch/start\_krebs

# Roche Group Media Office

Telephone: +41 61 688 8888 / Email: basel media office@roche.com

- Baschi Dürr
- Alexander Klauser
- Daniel Piller (Head Roche Group Media Office)
- Katja Prowald (Head Science Communications)
- Martina Rupp

References:
1. Boyle P, Ferlay J, Cancer incidence and mortality in Europe, 2004. Annals of Oncology 2005; 16:481-488
2. Boyle P, Languran JS, ABC of colorectal cancer. Epidemiology. BMJ 2000; 321:805-808

# Media Release

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Basel, 12 December 2006



Avastin shows positive outcomes in patients with advanced kidney cancer
Exciting new results add to Avastin's track record of success in patients with colorectal, lung and
breast cancer

An interim analysis of a phase III study in advanced renal cell cancer has shown that Avastin significantly prolongs the time patients live without their disease progressing. In addition, this early analysis indicated a trend towards an improvement in overall survival. Renal cell cancer is the most common form of kidney cancer accounting for nine out of ten cases and treatment options are limited. Due to the benefits observed, the independent Drug Safety Monitoring Board (DSMB) has recommended that the study be unblinded and all patients will be offered treatment with Avastin. Safety was in line with what has been observed for Avastin in previous studies.

"The results have shown that Avastin works effectively as a first-line treatment for renal cell cancer. This is the fourth cancer type in which Avastin's unique mode of action translates into a progression-free survival benefit for patients," said Eduard Holdener, Head of Roche Pharmaceuticals Development. "Current treatment options in advanced kidney cancer are limited and we are planning to work with health authorities in Europe to make Avastin available to patients with renal cell carcinoma as soon as possible."

In the AVOREN study patients received treatment with either Avastin and interferon alpha-2a or interferon alone, a standard of care in advanced kidney cancer. This is the first time that Avastin has demonstrated benefits for patients also in combination with an immunotherapeutic.

Further analyses of the AVOREN study are underway and results will be presented at an upcoming oncology conference.

## About AVOREN

AVOREN is an international phase III trial which included 649 patients with advanced renal cell cancer. Patients were divided into two arms to receive either standard therapy of interferon alpha-2a or interferon alpha-2a plus Avastin. Avastin was administered every two weeks at a dose of 10mg/kg. The primary endpoint of the study was to demonstrate overall survival when Avastin was added to interferon alpha-2a therapy. The study protocol specified an interim overall survival analysis be performed at approximately 50 percent of events. Secondary endpoints included progression free survival (PFS), time to progression, time to treatment failure, overall response rate and safety profile.

In line with previous feedback from health authorities, Roche is planning to file Avastin in Renal Cell Carcinoma based on results from the AVOREN study. In the US, in prior consultation with the FDA, the primary analysis endpoint was revised to assess improvement in PFS, defined as the length of time the rumour did not grow or patient death did not occur.

# About Kidney Cancer

On an annual basis in excess of 200,000 people will receive a diagnosis and more than 100,000 people will loose their lives to kidney cancer. This figure is expected to increase. Kidney cancer is more common in men than women (approximately 62% of renal cell carcinoma occurs in males) and incidence increases with age.

Renal cell carcinoma (RCC) is the most common type of kidney cancer, accounting for nine out of ten cases. If RCC is diagnosed at an early stage when the cancer is still confined to the kidney, the 5 year survival rates are relatively good at 60 – 75%. However, if diagnosis is made at a later stage and the cancer has already spread to distant sites the 5 year survival rate is less than 5%<sup>2</sup>. Unfortunately, because kidney cancer is often asymptomatic, the majority of patients are diagnosed at later disease stages.

Treatment options for patients with kidney cancer are limited. Surgical removal of part or the entire kidney forms the mainstay of treatment but is only really successful in early stage disease. In later stage disease, treatment is more often employed with a view of controlling the cancer and improving associated symptoms. These treatments are of limited success and include interferon alpha and interleukin or less commonly chemotherapy or radiotherapy.

#### About Avastin

Avastin is the first treatment that inhibits angiogenesis – the growth of a network of blood vessels that supply nutrients and oxygen to cancerous tissues. Avastin targets a naturally occurring protein called VEGF (Vascular Endothelial Growth Factor), a key mediator of angiogenesis, thus choking off the blood supply that is essential for the growth of the tumour and its spread throughout the body (metastasis).

Roche and Genentech are pursuing a comprehensive clinical programme investigating the use of Avastin in various tumour types (including colorectal, breast, lung, pancreatic cancer, ovarian cancer, renal cell carcinoma and others) and different settings (advanced and adjuvant ie post-operation). The total development programme is expected to include over 40,000 patients worldwide.

## About Roche

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## Additional information

- Roche in Oncology: www.roche.com/inboncology-e.pdf
- Roche Health Kiosk, Cancer: www.health-kiosk.ch/start\_krebs
- Avastin: www.avastin-info.com

Roche Group Media Office

Telephone: 141 61 688 8888 / Email: basel.mediaoffice@roche.com

- Baschi Dürr
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References

1 Parkin DM, Bray F, Ferlay J and Pisani P. Global cancer statistics 2002. CA Cancer J Clin 2005; 55; 74 – 108.

2 Medline Plus www.nlm.nih.gov/medlineplos/ency/article/000516.htm (accessed on 23rd October 2006)

# Investor Update

Furnished under Rule 12g3-2(b) ROCHE HOLDING 82-3315 Roche

DEC 2 1 2006

Basel, 12 December 2006

MabThera dramatically improves survival for first-line Non-Hodgkin Lymphoma patients

MabThera shown to be highly cost effective therapy for indolent NHL

Roche today announced exciting results from a pivotal phase III study that has followed the outcome of patients with follicular NHL, the most common form of indolent Non-Hodgkin's Lymphoma (iNHL), treated with MabThera more than four years ago. The follow-up study has shown that eight cycles of MabThera (rituximab) added to CVP chemotherapy in first line treatment significantly prolongs the overall survival when compared to chemotherapy alone. This study outcome, presented at the American Society of Hematology (ASH) meeting in Orlando, Florida, demonstrates for the first time clinically significant survival benefit in iNHL patients after 1st line treatment with MabThera / CVP combination therapy.

"These results represent a major advance in the treatment of indolent NHL," commented Dr Kevin Imrie, from Toronto-Sunnybrook Regional Cancer Center, a primary investigator of the study. "This is clear evidence that the addition of MabThera to first line chemotherapy for patients with indolent NHL not only extends the time that patients are free from the disease, but actually lengthens patients' lives!"

Non-Hodgkin's Lymphoma (NHL) affects 1 million people worldwide. It is estimated that 360,000 people die each year from the disease.<sup>2</sup> Indolent NHL, representing about 45% of NHL patients, is a slow developing but serious cancer of the lymphatic system.

The study demonstrated that a combination of eight-cycles of MabThera plus CVP (cyclophosphamide, vincristine and prednisolone) increased overall survival at 53 months - 81% of patients treated with MabThera were still alive compared with only 71% of patients who had only received chemotherapy (HR=0.60). This is the fourth phase III trial demonstrating overall survival benefit in indolent NHL with different combinations of MabThera and chemotherapy.

. ... . : 1.

The EU regulatory authorities approved MabThera in combination with CVP chemotherapy for the treatment of previously untreated patients with stage III-IV follicular NHL in 2004. The FDA approval for the same indication was received earlier this year.

# About the study

The multi-centre, phase III randomised study involved 321 patients from 11 countries and compared a treatment regimen of MabThera plus CVP chemotherapy with CVP chemotherapy alone. Patients were previously untreated and were diagnosed with advanced stage, indolent (follicular) NHL. Of the 321 patients involved, 159 were randomised into the CVP chemotherapy group and 162 into the MabThera plus CVP chemotherapy treatment group. Time to treatment failure was significantly prolonged by more than 1.5 years: 26 months versus 7 months; freedom from treatment progression was nearly doubled: 27 months versus 15 months.

# Pharmacoeconomic analyses shows MabThera cost effectivness

A pharmacoeconomic analysis, also presented today at the ASH meeting in Orlando, have demonstrated that MabThera (rituximab) is a highly cost effective treatment for maintenance therapy for patients with relapsed indolent NHL. The study³ was based on a Canadian pharmacoeconomic analysis of the European Organisation for Research and Treatment of Cancer (EORTC) 20981 trial, which demonstrated that MabThera maintenance therapy nearly halves the risk of death in patients when compared to observation. The pharmacoeconomic model showed that treatment with MabThera maintenance therapy was also highly cost effective, with an estimated increase both in overall survival (5.6 vs. 4.7 years) and QALYs (4.0 vs. 3.2 years) by almost a year, compared with chemotherapy alone.

# About MabThera

MabThera is a therapeutic antibody that binds to a particular protein - the CD20 antigen - on the surface of normal and malignant B-cells. It then recruits the body's natural defences to attack and kill the marked B-cells. Stem cells (B-cell progenitors) in bone marrow lack the CD20 antigen, allowing healthy B-cells to regenerate after treatment and return to normal levels within several months.

MabThera is indicated for the treatment of indolent and aggressive Non-Hodgkin's Lymphoma. MabThera is known as Rituxan in the United States, Japan and Canada. To date, patients have received more than 960,000 treatments with MabThera worldwide.

Genentech and Biogen Idec co-market MabThera in the United States, and Roche markets

MabThera in the rest of the world, except Japan, where MabThera is co-marketed by Chugai and

Zenyaku Kogyo Co. Ltd.

## About Roche

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#### Note to editors:

<sup>1</sup> Marcus et al, ASH 2006, Abstract #481

<sup>2</sup> Ferlay J, Bray F, Pisani P and Parkin D.M. GLOBOCAN 2002; Cancer Incidence, Mortality and Prevalence Worldwide IARC CancerBase No. 5, version 2.0 IARCPress, Lyon, 2004.

3 Maturi et al, ASH 2006, Abstract #343

#### Further Information:

- Roche in Oncology: www.roche.com/pages/downloads/company/pdf/mboncology05e b.pdf
- Lymphoma: www.lymphoma-net.org
- The Lymphoma Coalition: www.lymphomacoalition.org
- Cancer: www.health-kiosk.ch/start krebs.htm
- World Health Organization: www.who.int

#### Roche IR Contacts:

Dr. Karl Mahler

Phone: +41 (0)61 687 85 03

e-mail: karl.mahler@roche.com

Eva Schäfer-Jansen

Phone: +41 (0)61 688 66.36

e-mail: eva.schaefer-jansen@roche.com

Dianne Young

Phone: +41 (0)61 688 93 56

e-mail: dianne.young@roche.com

Dr. Zuzana Dobbie

Phone: +41 (0)61 688 80 27

e-mail: zuzana.dobbie@roche.com

Carla Bedard
Phone: +41 (0)61 687 13 00
e-mail: carla\_christine.bedard@roche.com

# North American investors please contact:

Thomas Kudsk Larsen
Phone: +41 (0)61 687 05 17
Mobile phone: +41 (0)79 829 15 07
e-mail: thomas\_kudsk.larsen@roche.com

# General inquiries:

International: +41 (0) 61 688 8880 North America: +1 973 562 2233 e-mail: investor.relations@roche.com



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DEC 2 1 2006

Basel, 13 December 2006

# Changes to the Roche Board of Directors and executive management

Reinforcement and further rejuvenation of Board and top management

Roche is reinforcing its Board of Directors with two experienced business leaders at the next shareholders' meeting and will move younger managers into key executive positions in 2007.

# Board of Directors to be expanded

At the next annual general meeting of Roche shareholders on 5 March 2007, the Board of Directors will propose that Pius Baschera and Wolfgang Ruttenstorfer be elected as additional members of the Board.

Prof. Pius Baschera, a Swiss citizen born in 1950, is currently chief executive of Hilti Corporation and designated chairman of the Hilti board. After completing degrees in mechanical engineering and management studies at the Swiss Federal Institute of Technology. Zurich, Baschera joined Hilti Corporation in 1979. He held a number of positions in the United States and Europe before being appointed CFO in 1990. In 1994 Prof. Baschera became chairman of the executive board, a position he will step down from when he becomes chairman of the board on 1 January 2007. Baschera is an honorary professor at the Swiss Federal Institute of Technology, Zurich.

Dr Wolfgang Ruttenstorfer, an Austrian citizen born in 1950, is a graduate of Vienna University of Economics and Business Administration. Since 2002 he has been CEO and chairman of the executive board of OMV Aktiengesellschaft, in addition to heading the company's natural gas and chemicals businesses. Ruttenstorfer joined OMV in 1976 and was appointed to the executive board in 1992. From 1997 to 1999 he was Austria's deputy minister of finance, returning to OMV in 2000. Ruttenstorfer is a recognised expert on the emerging markets of Eastern Europe and the Middle East.

# Changes to the Corporate Executive Committee

From 1 January 2007 Pascal Soriot, head of Pharma Strategic Marketing, will become head of Commercial Operations, with responsibility for Roche Pharmaceuticals' regional and country organisations and Strategic Marketing. As a new member of the Enlarged Corporate Executive Committee, he will continue to report directly to the CEO Division Roche Pharmaceuticals, William Burns.

Eduard Holdener, head of Global Pharma Development, will retire at the end of 2007. He will be succeeded by Jean-Jacques Garaud, who joins Roche on 1 January as a new member of the Pharma Executive Committee, reporting to William Burns. Until the end of the year, Ed Holdener will take over the function of Chief Medical Officer, with direct responsibility for Drug Safety and Quality Audit and for establishing a new development centre in Shanghai. All other Pharma Development functions will report to Jean-Jacques Garaud as of 1 January 2007.

Claude Schreiner, head of Roche Pharmaceuticals' Western Europe Region, will retire at the end of May 2007 after more than 40 years of service in key functions at Roche. He will be succeeded by Peter Hug, currently head of Pharma Partnering.

Roche would like to express its deep gratitude to Claude Schreiner and Eduard Holdener for their long and very valuable contributions to the company's success and wish them all the best for the future.

Announcing the changes, Roche Chairman and CEO Franz B. Humer said, "These new appointments continue the process we initiated a few years ago of systematically strengthening the Group's top echelons and bringing in new blood. It's been our policy for a good many years to promote young executives from within the company and to strengthen our organisation by recruiting recognised experts from outside. In terms of managerial and professional expertise, age structure and international experience, the Board, the Corporate Executive Committee and the top management of both divisions are now very well equipped to meet the challenges of the foture."

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# Roche Board of Directors and Corporate Executive Committee

# **Board of Directors**

Subject to approval of the nominees by the Annual General Meeting, from 5 March 2007 the membership of the Roche Board of Directors will be as follows:

Name, year of birth	Function	Term end	ls Elected
Dr Franz B. Humer (1946)	Chairman	2009	1995
Prof. Bruno Gehrig (1946)	Vice-Chairman, Independent Lead Director	2008	2004
André Hoffmann (1958)	Vice-Chairman	2009	1996
Prof. Pius Baschera (1950)*			2007*
Prof. John Irving Bell (1952)		2009	2001
Peter Brabeck-Letmathe (1944)		2010	2000
Lodewijk J.R. de Vink (1945)		2008	2004
Walter Frey (1943)		2008	2001
Dr DeAnne Julius (1949)		2010	2002
Dr Andreas Oeri (1949)	1	2008	1996
Wolfgang Ruttenstorfer (1950)	,		2007*
Prof. Florst Teltschik (1940)		2010	2002
Prof. Beatrice Weder di Mauro	(1965)	2010	2006
Dr Gottlieb A. Keller (1954)	Secretary to the Board of Directors		
Dr Fritz Gerber (1929)	Honorary Chairman of the Board of Directors		
"Subject to approval by the AGM			

# Corporate Executive Committee

From 2007, the membership of the Roche Corporate Executive Committee will be as follows:

Corporate Executive Committees	·
Franz B. Humer (1946)	Chairman and CEO of the Roche Group
Erich Hunziker (1953)	Chief Financial Officer, Deputy Head of the Corporate Executive
	Committee
William Burns (1947)	CEO Division Roche Pharmaceuticals
Severin Schwan (1967)	CEO Division Roche Diagnostics
Jonathan Knowles (1947)	Head of Global Research
Gottlieb Keller (1954)	Head of Corporate Services and Human Resources
Enlarged Corporate Executive Co	ommittee:
Ed Holdener (1945)*	Chief Medical Officer

Bolarged Corporate Executive Go	ommittee:
Ed Holdener (1945)*	Chief Medical Officer
Peter Hug (1958)**	Head of Pharma Partnering
Burkhard G. Piper (1961)	Head of Business Area Diabetes Care, Roche Diagnostics
Rolf Schläpfer (1956)	Head of Corporate Communications
Pascal Soriot (1959)	Head of Pharma Commercial Operations
Osamu Nagayama (1947)	President and CEO of Chugai Pharmaceutical Co., Ltd.

Secretary to the Corporate Executive Committee: Pierre Jaccoud (1955) Head of Ch Head of Chairman's Office

<sup>\*</sup> Member until 31 December 2007 \*\* Member until 31 May 2007

# Divisional executive management

From 2007, the membership of the Executive Committees of the Pharmaceuticals and Diagnostics Divisions will be as follows:

## Pharma Executive Committee:

William Burns (1947) George Abercrombie (1956) Jennifer Allerron (1951) Peter Hug (1958)

Jean-Jacques Garaud (1955) Eduard Holdener (1945) Jonathan Knowles (1947) Dominic Moorhead (1962) Paul Newton-Syms (1944) Claude Schreiner (1942) Pascal Soriot (1959) Jan van Koeveringe (1950) CEO Division Roche Pharmaceuticals
North America

Informatics

Pharma Partnering (until 31 May 2007) Western Europe (from 1 June 2007)

Development Chief Medical Officer

Research

Finance and Controlling

Human Resources

Western Europe (until 31 May 2007)

Commercial Operations Technical Operations

# Diagnostics Executive Committee:

Severin A. Schwan (1967)
Per-Olof Attinger (1960)
Silvia Ayyoubi (1953)
Manfred Baier (1951)
Christian Hebleh (1967)
Daniel O'Day (1964)
Tiffony Olson (1959)
Volker Pfahlert (1958)
Burkhard G. Piper (1961)
Jürgen Schwiczer (1944)
Robert Yates (1958)

CEO Division Roche Diagnostics
Platforms & Support
Human Resources
Applied Science
Finance & Services
Molecular Diagnostics
Region North America
Professional Diagnostics
Diabetes Care

EMEA and Latin America Business Development

# Biographies

Jean-Jacques Garaud, a French citizen born in 1955, completed a medical degree and held several university and hospital posts before moving to the pharmaceutical industry in 1985. He worked in clinical research with Marion Merrel Dow, Rhône-Poulenc Rorer und Schering-Plough. Garaud joined Novartis in 2002, becoming global head of Exploratory Development in 2005.

Peter Hug, a Swiss citizen born in 1958, has a PhD in economics and began his career at Roche in 1983. Hug worked in several pharmaceuticals marketing roles in Switzerland, Canada and Greece before holding positions as General Manager in Uruguay, Switzerland and Spain. In addition, for two years he was head of Roche's diagnostics business in Germany. Hug has been head of Pharma Partnering since 2004.

Pascal Soriot, a French citizen biorn in 1959, holds a doctorate in veterinary medicine and an MBA from HEC Paris. In a career with Sanofi-Aventis lasting 20 years he held management positions in

France, Australia, New Zealand, Asia-Pacific and the United States. Soriot joined Roche in 2006 as head of Pharma Strategic Marketing.

# Media Relations Contacts

Phone: 441 61 688 88 88 / c-mail: basel.mediaoffice@roche.com

- Baschi Dürr
- · Alexander Klauser
- Daniel Piller (Head Roche Group Media Office)
- Katja Prowald (Head Science Communications)
- Martina Rupp

# Investor Update

Furnished under Rule 12g3-2(b) ROCHE HOLDING 82-3315





Basel, 15 December 2006

# Roche offers the FDA additional Mircera data FDA accepts and grants three month extension to the review

Roche today announced that it has submitted additional data to the FDA to support its Biologic Licence Application (BLA) for Mircera. These data offered are intended to provide as comprehensive an understanding of Mircera as is possible to assist the FDA in completing the review process. As a result of this action, the FDA has granted Roche a three month extension to the review period.

"The newly available Mircera data that we have proactively submitted will help to give the FDA additional clarity in key areas that the FDA is monitoring with already available anti-anaemia agents," said Eduard Holdener, Global Head Pharma Development. He added: "We want to ensure that our application to the FDA is as robust as possible in an evolving regulatory environment and we are confident that the additional data submitted will facilitate a positive review of Mircera."

Roche is seeking an indication for Mircera in the treatment of anaemia associated with chronic kidney disease (CKD) including patients on dialysis or not on dialysis. The BLA submitted to the FDA is based on data from all six studies that comprise the Phase III clinical program. This included treating anaemia in previously untreated patients and maintaining haemoglobin (Hb) after conversion from epoetin alfa/beta or darbepoetin alfa. The program consisted of two treatment/correction and four conversion/maintenance studies of both intravenous and subcutaneous Mircera at extended administration intervals of up to once monthly.

## About Mircera

Mircera is a new anti-anaemia agent. It is both functionally and structurally unique. It is the first continuous erythropoietin receptor activator and it differs from rhuEPO by being a complex, chemically synthesized erythropoiesis stimulating agent. Mircera differs from existing ESAs by its mechanism of action; long half-life; and by being the first new anti-anaemia agent which was

specifically designed to provide long dosing intervals of up to once a month. If approved, it will be the first agent to correct anaemia in chronic kidney disease patients on dialysis and not on dialysis with dosing once every two weeks and the first to maintain these patients on dosing intervals up to once a month. Mircera is also the first drug to have compared itself in clinical trials against all available agents: epoetin alfa, beta and darbepoetin alfa.

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# Roche IR Contacts:

Dr. Karl Mahler Phone: +41 (0)61 687 85 03

e-mail: karl.mahler@roche.com

Dianne Young

Phone: +41 (0)61 688 93 56

e-mail: dianne.young@roche.com

Carla Bedard

Phone: +41 (0)61 687 13 00

e-mail: carla\_christine.bedard@roche.com

North American investors please contact:

Thomas Kudsk Larsen Phone: +41 (0)61 687 05 17

Mobile phone: +41 (0)79 829 15 07 e-mail: thomas\_kudsk.larsen@roche.com Eva Schäfer-Jansen

Phone: +41 (0)61 688 66 36

e-mail: eva.schaefer-jansen@roche.com

Dr. Zuzana Dobbie

Phone: +41 (0)61 688 80 27

e-mail: zuzana.dobbie@roche.com

# General inquiries:

International: +41 (0) 61 688 8880 North America: +1 973 562 2233 e-mail: investor.relations@roche.com

# Investor Update

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# Landmark study of Avastin in lung cancer published today in New England Journal of Medicine

Avastin is first medicine to extend survival beyond one year in patients with previously untreated non-small cell lung cancer

Avastin is the first medicine proven to help previously untreated patients suffering from the most common form of lung cancer to live longer than a year, according to a landmark US study (E4599) published today in the prestigious New England Journal of Medicine.

The study showed that the median duration of survival in the Avastin plus paclitaxel and carboplatin chemotherapy group was 12.3 months compared to 10.3 months in the group treated with chemotherapy alone. Overall patients treated with Avastin plus chemotherapy had an approximate 27 percent improvement in survival compared to patients receiving chemotherapy alone.

"This is the first large, randomized clinical study in which an anti-angiogenic, combined with chemotherapy, extended survival beyond one year in patients with advanced lung cancer," said Alan B. Sandler, M.D., director of Medical Thoracic Oncology at Vanderbilt-Ingram Cancer Center in Nashville, Tenn., and Study Chair for the E4599 trial. "The results of this study have changed the treatment standard of care for this devastating disease - an important step forward for patients with advanced lung cancer."

The results from the pivotal study highlight the outstanding achievements of Roche's innovative cancer medicine Avastin in helping people with previously untreated advanced NSCLC. Lung cancer is the most common form of cancer as well as the single biggest cancer killer with more than 900 lives lost to the disease every day in Europe and new treatment options are desperately needed.

The impressive data from the E4599 study formed the basis for the US approval of Avastin for treatment of advanced NSCLC which was granted by the FDA in October 2006. For the European filing which was submitted on 8 August 2006, the E4599 study was supported by the preliminary data from the ongoing "Avastin in Lung" (BO17704) study.

F. Hoffmann-La Roche Ltd

CH-4070 Basel

Investor Relations

Tel. +41-(0)61-688 88 80

Locally advanced, metastatic or recurrent non-small cell lung cancer (NSCLC) with histology other than predominant squamous cell

Avastin was approved in the EU in January 2005 and in the US in February 2004 for the first-line treatment of patients with metastatic colorectal cancer. It received another approval in the US in June 2006 as a second-line treatment for patients with metastatic colorectal cancer. The first filing for Avastin in Japan occurred in April 2006 for the treatment of metastatic colorectal cancer. More recently, Avastin was filed for the treatment of women with advanced breast cancer in the EU in July 2006.

# About the pivotal E4599 study

The results of the randomised, controlled, multicenter Phase III E4599 study of 878 patients with locally advanced, metastatic or recurrent NSCLC, with histology other than predominant squamous cell, show that:

- Median survival of patients treated with Avastin at a dose of 15 mg/kg every three weeks plus chemotherapy was 12.3 months, compared to 10.3 months for patients treated with chemotherapy alone
- Patients receiving Avastin at a dose of 15 mg/kg every three weeks plus paclitaxel and carboplatin had an approximate 27 percent improvement in overall survival, compared to patients who received chemotherapy alone
- Median duration of progression-free survival (measure of the time patients live without their disease progressing) was 6.2 months for patients treated with Avastin plus chemotherapy, compared to 4.5 months for patients treated with chemotherapy alone
- Response rate in patients with measurable disease was more than doubled to 35 percent in the group receiving Avastin plus chemotherapy, compared to 15 percent in the group receiving chemotherapy alone
- Side effects were generally manageable. Pulmonary haemorrhage (haemoptysis) cases were observed in 1.9% of the patients receiving Avastin plus chemotherapy. The most common adverse events associated with Avastin monotherapy were: hypertension (5.6%), proteinuria (4.2%), fatigue (5.1%) and dyspnoea (5.6%)

# **About Avastin**

Avastin is the first treatment that inhibits angiogenesis – the growth of a network of blood vessels that supplies nutrients and oxygen to cancerous tissues. Avastin targets a naturally occurring protein called VEGF (Vascular Endothelial Growth Factor), a key mediator of angiogenesis, thus choking off the blood supply that is essential for the growth of the tumour and its spread throughout the body (metastasis).

Avastin is the first and only anti-angiogenic agent to have demonstrated improved overall and/or progression-free survival in four major tumour types, namely: colorectal cancer, non-small cell lung

cancer, breast cancer and renal cell carcinoma.

Roche and Genentech are pursuing a comprehensive clinical programme investigating the use of Avastin in various tumour types (including colorectal, breast, lung, pancreatic cancer, ovarian cancer, renal cell carcinoma and others) and different settings (advanced and adjuvant i.e. post-operation). The total development programme is expected to include over 40,000 patients worldwide.

# **About Roche**

Headquartered in Basel, Switzerland, Roche is one of the world's leading research-focused healthcare groups in the fields of pharmaceuticals and diagnostics. As a supplier of innovative products and services for the early detection, prevention, diagnosis and treatment of disease, the Group contributes on a broad range of fronts to improving people's health and quality of life. Roche is a world leader in diagnostics, the leading supplier of medicines for cancer and transplantation and a market leader in virology. In 2005 sales by the Pharmaceuticals Division totalled 27.3 billion Swiss francs, and the Diagnostics Division posted sales of 8.2 billion Swiss francs. Roche employs roughly 70,000 people in 150 countries and has R&D agreements and strategic alliances with numerous partners, including majority ownership interests in Genentech and Chugai. Additional information about the Roche Group is available on the Internet (www.roche.com).

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#### Additional information

- Roche in Oncology: www.roche.com/pages/downloads/company/pdf/mboncology05e b.pdf
- Roche Health Kiosk, Cancer: www.health-kiosk.ch/start\_krebs
- Avastin: www.avastin.com

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## Roche IR Contacts:

Dr. Karl Mahler

Phone: +41 (0)61 687 85 03

e-mail: karl.mahler@roche.com

mail: karl.mahler@rocne.com

Eva Schäfer-Jansen

Phone: +41 (0)61 688 66 36

e-mail: eva.schaefer-jansen@roche.com

Dianne Young

Phone: +41 (0)61 688 93 56

e-mail: dianne.young@roche.com

Dr. Zuzana Dobbie

Phone: +41 (0)61 688 80 27

e-mail: zuzana.dobbie@roche.com

Carla Bedard

Phone: +41 (0)61 687 13 00

e-mail: carla\_christine.bedard@roche.com

# North American investors please contact:

Thomas Kudsk Larsen
Phone: +41 (0)61 687 05 17
Mobile phone: +41 (0)79 829 15 07
e-mail: thomas\_kudsk.larsen@roche.com

# General inquiries:

International: +41 (0) 61 688 8880 North America: +1 973 562 2233 e-mail: investor.relations@roche.com

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